

addition of claims) are hereby authorized to be charged to our Deposit Account No. 19-0036.

### ***Amendments to the Claims***

The listing of claims will replace all prior versions, and listings of claims in the application.

Claim 1 (currently amended). A method of treating[[,]] or ameliorating ~~or preventing~~ a disease or condition caused by exposure to radionuclides, biological agents, or chemical agents in an animal, comprising administering to an animal in need thereof an effective amount of a caspase inhibitor such that cell death in response to said exposure to said radionuclides, biological agents, or chemical agents is inhibited;

wherein said biological agent is selected from the group consisting of anthrax, botulinum, aflatoxin, Clostridium, plague, Cornelia, Ebola, Marburg, Staphylococcus, Streptococcus, ricin, modeccin, diphtheria, Pseudomonas, and cholera; and

wherein said chemical agent is selected from the group consisting of nitrogen mustard and cyanide;

with the proviso that said radionuclide is not a measured dose of radiation for cancer therapy.

Claim 2 (original). The method of claim 1, wherein said cell death occurs in cells of the gastrointestinal tract, skin, hair, bone marrow, immune system, nervous system or liver.

Claim 3 (original). The method of claim 1, wherein said caspase inhibitor is administered topically or orally.

Claim 4 (original). The method of claim 1, wherein said caspase inhibitor is administered systemically by intravenous, intraperitoneal, intramuscular, or subcutaneous injection.

Claim 5 (original). The method of claim 1, wherein said caspase inhibitor is administered as part of a pharmaceutical composition comprising a pharmaceutically acceptable carrier.

Claim 6 (original). The method of claim 1, wherein said exposure to radionuclides, biological agents, or chemical agents is unintentional.

Claim 7 (original). The method of claim 6, wherein said radionuclides, biological agents, or chemical agents are from a nuclear power plant, manufacturing or processing plant, research facility, or hospital.

Claim 8 (original). The method of claim 1, wherein said exposure to radionuclides, biological agents, or chemical agents is intentional.

Claim 9 (original). The method of claim 8, wherein said radionuclides, biological agents, or chemical agents are from a spill or a bomb.

Claim 10 (original). The method of claim 1, wherein said radionuclides are part of a radiopharmaceutical agent.

Claim 11 (original). The method of claim 1, wherein said radionuclides are selected from the group consisting of actinium ( $^{225}\text{Ac}$ ), americium ( $^{241}\text{Am}$ ), antimony ( $^{124}\text{Sb}$ ,  $^{125}\text{Sb}$ ), arsenic ( $^{72}\text{As}$ ,  $^{73}\text{As}$ ,  $^{74}\text{As}$ ), astatine ( $^{211}\text{At}$ ), barium ( $^{103}\text{Ba}$ ,  $^{140}\text{Ba}$ ), beryllium ( $^7\text{Be}$ ), bismuth ( $^{206}\text{Bi}$ ,  $^{207}\text{Bi}$ ,  $^{212}\text{Bi}$ ,  $^{213}\text{Bi}$ ), bromine ( $^{77}\text{Br}$ ), cadmium ( $^{109}\text{Cd}$ ,  $^{115}\text{Cd}$ ), calcium ( $^{45}\text{Ca}$ ), carbon ( $^{14}\text{C}$ ), cerium ( $^{139}\text{Ce}$ ,  $^{141}\text{Ce}$ ,  $^{144}\text{Ce}$ ), cesium ( $^{129}\text{Cs}$ ,  $^{137}\text{Cs}$ ), chromium ( $^{51}\text{Cr}$ ,  $^{56}\text{Cr}$ ), cobalt ( $^{55}\text{Co}$ ,  $^{56}\text{Co}$ ,  $^{57}\text{Co}$ ,  $^{58}\text{Co}$ ,  $^{60}\text{Co}$ ,  $^{64}\text{Co}$ ), copper ( $^{61}\text{Cu}$ ,  $^{64}\text{Cu}$ ,  $^{67}\text{Cu}$ ), erbium ( $^{169}\text{Er}$ ), europium ( $^{152}\text{Eu}$ ), fluorine ( $^{18}\text{F}$ ), gadolinium ( $^{153}\text{Gd}$ ), gallium

(<sup>67</sup>Ga, <sup>68</sup>Ga), gold (<sup>195</sup>Au, <sup>198</sup>Au, <sup>199</sup>Au), hafnium (<sup>175</sup>Hf, <sup>181</sup>Hf), holmium (<sup>166</sup>Ho), hydrogen (<sup>3</sup>H), krypton (<sup>85</sup>Kr), iodine (<sup>123</sup>I, <sup>125</sup>I, <sup>126</sup>I, <sup>131</sup>I, <sup>133</sup>I), indium (<sup>111</sup>In, <sup>113</sup>In), iridium (<sup>192</sup>Ir), iron (<sup>52</sup>Fe, <sup>55</sup>Fe, <sup>59</sup>Fe), lead (<sup>203</sup>Pb, <sup>210</sup>Pb, <sup>212</sup>Pb), lutetium (<sup>177</sup>Lu), magnesium (<sup>52</sup>Mg), manganese (<sup>54</sup>Mn), mercury (<sup>197</sup>Hg, <sup>203</sup>Hg), molybdenum (<sup>99</sup>Mo), neodymium (<sup>147</sup>Nd), neptunium (<sup>237</sup>Np), nickel (<sup>57</sup>Ni, <sup>63</sup>Ni), niobium (<sup>95</sup>Nb), osmium (<sup>185</sup>Os, <sup>191</sup>Os), palladium (<sup>103</sup>Pd, <sup>109</sup>Pd), phosphorus (<sup>32</sup>P, <sup>33</sup>P), platinum (<sup>195</sup>Pt, <sup>197</sup>Pt), plutonium (<sup>239</sup>Pu), potassium (<sup>40</sup>K), praseodymium (<sup>142</sup>Pr, <sup>143</sup>Pr), promethium (<sup>147</sup>Pm), protactinium (<sup>233</sup>Pa), radium (<sup>223</sup>Ra, <sup>226</sup>Ra), rhenium (<sup>186</sup>Re, <sup>188</sup>Re), rhodium (<sup>105</sup>Rh), rubidium (<sup>81</sup>Rb, <sup>86</sup>Rb), ruthenium (<sup>95</sup>Ru, <sup>97</sup>Ru, <sup>103</sup>Ru, <sup>105</sup>Ru, <sup>106</sup>Ru), samarium (<sup>153</sup>Sm), scandium (<sup>44</sup>Sc, <sup>46</sup>Sc, <sup>47</sup>Sc), selenium (<sup>72</sup>Se, <sup>73</sup>Se, <sup>75</sup>Se), silver (<sup>100</sup>Ag, <sup>111</sup>Ag), sodium (<sup>22</sup>Na), strontium (<sup>85</sup>Sr, <sup>89</sup>Sr, <sup>90</sup>Sr), sulfur (<sup>35</sup>S), tantalum (<sup>179</sup>Ta, <sup>182</sup>Ta), technetium (<sup>99</sup>Tc), tellurium (<sup>121</sup>Te, <sup>122</sup>Te, <sup>125</sup>Te, <sup>132</sup>Te), terbium (<sup>161</sup>Tb), thallium (<sup>170</sup>Tl, <sup>201</sup>Tl, <sup>204</sup>Tl), thorium (<sup>228</sup>Th, <sup>230</sup>Th, <sup>232</sup>Th), thulium (<sup>165</sup>Tm, <sup>167</sup>Tm, <sup>168</sup>Tm, <sup>170</sup>Tm), tin (<sup>113</sup>Sn), titanium (<sup>44</sup>Ti), tungsten (<sup>185</sup>W), uranium (<sup>233</sup>U, <sup>235</sup>U, <sup>238</sup>U), vanadium (<sup>48</sup>V, <sup>49</sup>V), ytterbium (<sup>169</sup>Yb), yttrium (<sup>88</sup>Y, <sup>90</sup>Y, <sup>91</sup>Y), zinc (<sup>62</sup>Zn, <sup>65</sup>Zn) and zirconium (<sup>95</sup>Zr).

Claim 12 (currently amended). A method of treating or ameliorating a disease or condition caused by exposure to biological agents in an animal, comprising administering to an animal in need thereof an effective amount of a caspase inhibitor such that cell death in response to said exposure to said biological agents is inhibited; ~~The method of claim 1, wherein said biological agents are selected from the group consisting of anthrax and its toxins, botulinum and its toxins, aflatoxin, sterigmatocystin, deoxynivalenol, fumonisin B1, *Clostridium difficile* and its toxins, plague (*Yersinia pestis*) and its toxins, hemorrhagic fevers, *Staphylococcus aureus*, Streptococcus, ricin, modeccin, diphtheria, and Pseudomonas, and cholera and its toxins.~~

Claim 13 (currently amended). A method of treating or ameliorating a disease or condition caused by exposure to chemical agents in an animal, comprising administering to an animal in need thereof an effective amount of a caspase inhibitor such that cell death in response to said exposure to said chemical agents is inhibited; ~~The method of claim 1, wherein said chemical agents are selected from the group consisting~~

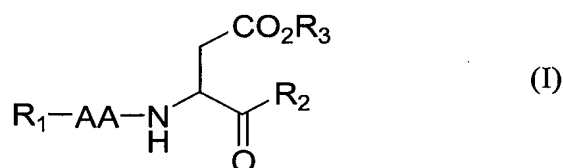
of ~~phosphoramidate mustard, melphalan, chlorambucil, quinaerine mustard,~~ nitrogen mustard, ~~cyclophosphamide, 4-hydroxycyclophosphamide,~~ and cyanide.

Claim 14 (original). The method of claim 1, wherein said caspase inhibitor is administered after exposure to radionuclides, biological agents, or chemical agents in said animal.

Claim 15 (original). The method of claim 1, wherein said caspase inhibitor is administered during exposure to radionuclides, biological agents, or chemical agents in said animal.

Claim 16 (original). The method of claim 1, wherein said caspase inhibitor is administered prior to exposure to radionuclides, biological agents, or chemical agents in said animal.

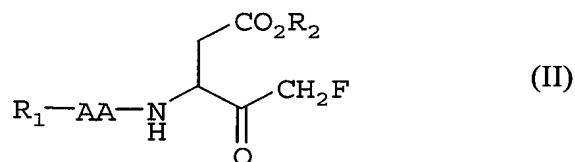
Claim 17 (original). The method of claim 1, wherein said caspase inhibitor has the formula:



or a pharmaceutically acceptable salt thereof;  
wherein R<sub>1</sub> is an N-terminal protecting group;  
AA is a residue of any natural or non-natural α-amino acid, β-amino acid, derivatives of an α-amino acid or β-amino acid;  
R<sub>2</sub> is H or CH<sub>2</sub>R<sub>4</sub> where R<sub>4</sub> is an electronegative leaving group; and  
R<sub>3</sub> is alkyl or H.

Claim 18 (original). The method of claim 17, wherein said caspase inhibitor is Boc-Ala-Asp-CH<sub>2</sub>F, Boc-Val-Asp-CH<sub>2</sub>F, Boc-Leu-Asp-CH<sub>2</sub>F, Ac-Val-Asp-CH<sub>2</sub>F, Ac-Ile-Asp-CH<sub>2</sub>F, Ac-Met-Asp-CH<sub>2</sub>F, Cbz-Val-Asp-CH<sub>2</sub>F, Cbz-β-Ala-Asp-CH<sub>2</sub>F, Cbz-Leu-Asp-CH<sub>2</sub>F, Cbz-Ile-Asp-CH<sub>2</sub>F, Boc-Ala-Asp(OMe)-CH<sub>2</sub>F, Boc-Val-Asp(OMe)-CH<sub>2</sub>F, Boc-Leu-Asp(OMe)-CH<sub>2</sub>F, Ac-Val-Asp(OMe)-CH<sub>2</sub>F, Ac-Ile-Asp(OMe)-CH<sub>2</sub>F, Ac-Met-Asp(OMe)-CH<sub>2</sub>F, Cbz-Val-Asp(OMe)-CH<sub>2</sub>F, Cbz-β-Ala-Asp(OMe)-CH<sub>2</sub>F, Cbz-Leu-Asp(OMe)-CH<sub>2</sub>F or Cbz-Ile-Asp(OMe)-CH<sub>2</sub>F.

Claim 19 (original). The method of claim 1, wherein said caspase inhibitor has the formula II:



or a pharmaceutically acceptable salt thereof;

wherein R<sub>1</sub> is an N-terminal protecting group;

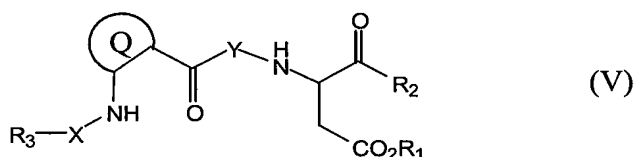
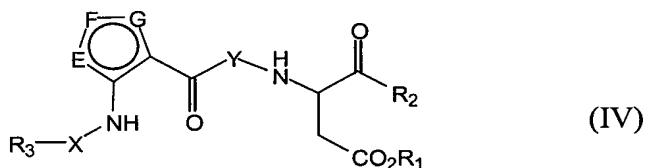
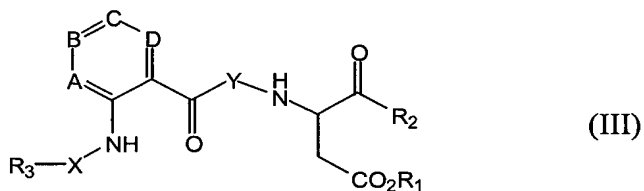
AA is a residue of a non-natural α-amino acid or β-amino acid; and

R<sub>2</sub> is an optionally substituted alkyl or H.

Claim 20 (withdrawn). The method of claim 19, wherein said caspase inhibitor is Boc-Phg-Asp-fmk, Boc-(2-F-Phg)-Asp-fmk, Boc-(F<sub>3</sub>-Val)-Asp-fmk, Boc-(3-F-Val)-Asp-fmk, Ac-Phg-Asp-fmk, Ac-(2-F-Phg)-Asp-fmk, Ac-(F<sub>3</sub>-Val)-Asp-fmk, Ac-(3-F-Val)-Asp-fmk, Z-Phg-Asp-fmk, Z-(2-F-Phg)-Asp-fmk, Z-(F<sub>3</sub>-Val)-Asp-fmk, Z-Chg-Asp-fmk, Z-(2-Fug)-Asp-fmk, Z-(4-F-Phg)-Asp-fmk, Z-(4-Cl-Phg)-Asp-fmk, Z-(3-Thg)-Asp-fmk, Z-(2-Fua)-Asp-fmk, Z-(2-Tha)-Asp-fmk, Z-(3-Fua)-Asp-fmk, Z-(3-Tha)-Asp-fmk, Z-(3-Cl-Ala)-Asp-fmk, Z-(3-F-Ala)-Asp-fmk, Z-(F<sub>3</sub>-Ala)-Asp-fmk, Z-(3-F-3-Me-Ala)-Asp-fmk, Z-(3-Cl-3-F-Ala)-Asp-fmk, Z-(2-Me-Val)-Asp-fmk, Z-(2-Me-Ala)-Asp-fmk, Z-(2-*i*-Pr-β-Ala)-Asp-fmk, Z-(3-Ph-β-Ala)-Asp-fmk, Z-(3-CN-Ala)-Asp-fmk, Z-(1-Nal)-Asp-fmk, Z-Cha-Asp-fmk, Z-(3-CF<sub>3</sub>-Ala)-Asp-fmk, Z-(4-CF<sub>3</sub>-Phg)-Asp-fmk,

Z-(3-Me<sub>2</sub>N-Ala)-Asp-fmk, Z-(2-Abu)-Asp-fmk, Z-Tle-Asp-fmk, Z-Cpg-Asp-fmk, Z-Cbg-Asp-fmk, Z-Thz-Asp-fmk, Z-(3-F-Val)-Asp-fmk, or Z-(2-Thg)-Asp-fmk.

Claim 21 (original). The method of claim 1, wherein said caspase inhibitor has the formula of one of III, IV and V:



or a pharmaceutically acceptable salt thereof;

wherein R<sub>1</sub> is an optionally substituted alkyl or hydrogen,

R<sub>3</sub> is an N-protecting group;

R<sub>2</sub> is hydrogen or optionally substituted alkyl;

A is CR<sub>6</sub> or nitrogen;

B is CR<sub>7</sub> or nitrogen;

C is CR<sub>8</sub> or nitrogen;

D is CR<sub>9</sub> or nitrogen;

provided that not more than two of A, B, C or D is nitrogen; and

R<sub>6</sub>-R<sub>9</sub> independently are hydrogen, halo, C<sub>1</sub>-C<sub>6</sub> haloalkyl, C<sub>6</sub>-C<sub>10</sub> aryl, C<sub>4</sub>-C<sub>7</sub> cycloalkyl, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, C<sub>6</sub>-C<sub>10</sub> aryl(C<sub>1</sub>-C<sub>6</sub>)alkyl, C<sub>6</sub>-C<sub>10</sub> aryl(C<sub>2</sub>-C<sub>6</sub>)alkenyl, C<sub>6</sub>-C<sub>10</sub> aryl(C<sub>2</sub>-C<sub>6</sub>)alkynyl; C<sub>1</sub>-C<sub>6</sub> hydroxyalkyl, nitro, amino, cyano, C<sub>1</sub>-C<sub>6</sub> acylamino, hydroxy, C<sub>1</sub>-C<sub>6</sub> acyloxy, C<sub>1</sub>-C<sub>6</sub> alkoxy, alkylthio, or carboxy; or

one of R<sub>6</sub> and R<sub>7</sub>, or R<sub>7</sub> and R<sub>8</sub>, or R<sub>8</sub> and R<sub>9</sub> are taken together with the carbon atoms to which they are attached to form a carbocycle or heterocycle;

E is CR<sub>14</sub>, nitrogen, oxygen or sulfur;

F is CR<sub>15</sub>, nitrogen, oxygen or sulfur;

G is C<sub>16</sub>, nitrogen, oxygen or sulfur;

provided that only one of E, F, G is nitrogen, oxygen or sulfur, where R<sub>14</sub>-R<sub>16</sub> are independently hydrogen, halo, C<sub>1</sub>-C<sub>6</sub> haloalkyl, C<sub>6</sub>-C<sub>10</sub> aryl, C<sub>4</sub>-C<sub>7</sub> cycloalkyl, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, C<sub>6</sub>-C<sub>10</sub> aryl(C<sub>1</sub>-C<sub>6</sub>)alkyl, C<sub>6</sub>-C<sub>10</sub> aryl(C<sub>2</sub>-C<sub>6</sub>)alkenyl, C<sub>6</sub>-C<sub>10</sub> aryl(C<sub>2</sub>-C<sub>6</sub>)alkynyl; C<sub>1</sub>-C<sub>6</sub> hydroxyalkyl, nitro, amino, cyano, C<sub>1</sub>-C<sub>6</sub> acylamino, hydroxy, C<sub>1</sub>-C<sub>6</sub> acyloxy, C<sub>1</sub>-C<sub>6</sub> alkoxy, alkylthio, or carboxy; or

one of R<sub>14</sub> and R<sub>15</sub>, or R<sub>15</sub> and R<sub>16</sub>, are taken together with the carbon atoms to which they are attached to form a carbocycle or heterocycle;

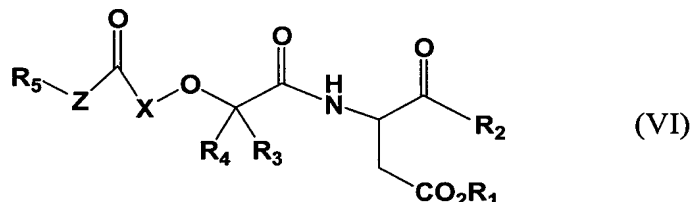
Q represents an optionally substituted saturated or partially saturated carbocycle or heterocycle;

X is a peptide of 1-4 amino acids or a bond; and

Y is a peptide of 1-4 amino acids or a bond.

Claim 22 (withdrawn). The method of claim 21, wherein said caspase inhibitor is 2-(Z-amino)benzoyl-Asp-fmk, 2-(Z-amino)-3-methylbenzoyl-Asp-fmk, 2-(Z-amino)-3,5-dimethylbenzoyl-Asp-fmk, 2-(Z-amino)-4-chlorobenzoyl-Asp-fmk, 2-(Z-amino)-5-chlorobenzoyl-Asp-fmk, 2-(Z-amino)-5-fluorobenzoyl-Asp-fmk, 2-(Z-amino)-6-fluorobenzoyl-Asp-fmk, cis-2-(Z-amino)cyclohexanecarboxyl-Asp-fmk, 2-(Z-amino)-5-methylbenzoyl-Asp-fmk, 2-(Z-amino)-6-methylbenzoyl-Asp-fmk, 2-(Z-amino)-6-chlorobenzoyl-Asp-fmk, 2-(Z-amino)-3-methoxybenzoyl-Asp-fmk, 2-(Z-amino)thiophene-2-carboxyl-Asp-fmk, 2-(methoxycarbonylamino)thiophene-2-carboxyl-Asp-fmk, cis-2-(Z-amino)cyclopentanecarboxyl-Asp-fmk, trans-2-(Z-amino)cyclopentanecarboxyl-Asp-fmk, 2-(Z-amino)benzoyl-Asp-DCB-methylketone, methoxycarbonyl-Val-(2-aminobenzoyl)-Asp-fmk, Z-Glu-(2-aminobenzoyl)-Asp-fmk or Z-Val-(2-aminobenzoyl)-Asp-fmk.

Claim 23 (original). The method of claim 1, wherein said caspase inhibitor has the formula VI:



or a pharmaceutically acceptable salt thereof, wherein

R<sub>1</sub> is an optionally substituted alkyl or hydrogen;

R<sub>2</sub> is hydrogen or optionally substituted alkyl;

R<sub>3</sub> and R<sub>4</sub> independently are hydrogen, optionally substituted aryl, optionally substituted heterocyclic, optionally substituted carbocyclic, optionally substituted heteroaryl, optionally substituted alkyl, optionally substituted alkenyl, or optionally substituted alkynyl;

R<sub>5</sub> is an optionally substituted alkyl, optionally substituted carbocyclic, optionally substituted heterocyclic, optionally substituted aryl or optionally substituted heteroaryl;

Z is O, S, NR<sub>8</sub>, or (CR<sub>9</sub>R<sub>10</sub>)<sub>n</sub>, where R<sub>8</sub>, R<sub>9</sub> and R<sub>10</sub> independently are hydrogen, alkyl or cycloalkyl, and n is 0, 1, 2, or 3; and

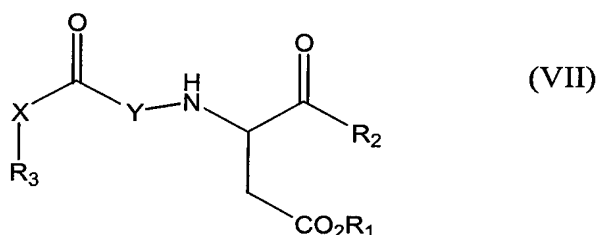
X is a peptide of 1-2 amino acids or a bond.

Claim 24 (withdrawn). The method of claim 23, wherein said caspase inhibitor is 1-(Carbonyl-Asp-CH<sub>2</sub>F)ethyl N-phenylcarbamate, 1-(Carbonyl-Asp-CH<sub>2</sub>F)ethyl N-benzylcarbamate, 2-Methyl-1-(carbonyl-Asp-CH<sub>2</sub>F)propyl N-phenylcarbamate, 2-Methyl-1-(carbonyl-Asp-CH<sub>2</sub>F)propyl N-benzylcarbamate, 2-Methyl-1-(carbonyl-Asp-CH<sub>2</sub>F)propyl N-(2,6-dichlorophenyl)carbamate, 2-Methyl-1-(carbonyl-Asp-CH<sub>2</sub>F)propyl N-(2,5-dichlorophenyl)-carbamate, 2-Methyl-1-(carbonyl-Asp-CH<sub>2</sub>F)propyl N-(2,4-dichlorophenyl)-carbamate, 2-Methyl-1-(carbonyl-Asp-CH<sub>2</sub>DCB)propyl N-phenylcarbamate, 2-Methyl-1-(carbonyl-Asp-CH<sub>2</sub>DCB)propyl N-(2,6-dichlorophenyl)-carbamate, 2-Methyl-1-(carbonyl-Asp-CH<sub>2</sub>PTP)propyl N-phenylcarbamate, 2-Methyl-1-(carbonyl-Asp-CH<sub>2</sub>PTP)propyl N-(2,6-dichlorophenyl)-



carbamate, 2-Methyl-1-(carbonyl-Asp-CH<sub>2</sub>DPP)propyl *N*-phenylcarbamate, 2-Methyl-1-(carbonyl-Asp-CH<sub>2</sub>DPP)propyl *N*-(2,6-dichlorophenyl)-carbamate, 2-Methyl-1-(carbonyl-Asp-CH<sub>2</sub>F)propyl *N*-(2-methyl-1-methoxycarbonyl-propyl)carbamate, 2-Methyl-1-(carbonyl-Asp-CH<sub>2</sub>F)propyl *N*-(3-fluorophenyl)carbamate, 2-Methyl-1-(carbonyl-Asp-CH<sub>2</sub>F)propyl *N*-(4-fluorophenyl)carbamate, 2-Methyl-1-(carbonyl-Asp-CH<sub>2</sub>F)propyl *N*-(3,4-difluorophenyl)carbamate, 2-Methyl-1-(carbonyl-Asp-CH<sub>2</sub>F)propyl *N*-(4-phenoxyphenyl)carbamate, 1-(Carbonyl-Asp-CH<sub>2</sub>F)propyl *N*-phenylcarbamate, 1-(Carbonyl-Asp-CH<sub>2</sub>F)butyl *N*-phenylcarbamate, 1-(Carbonyl-Asp-CH<sub>2</sub>F)-2-propenyl *N*-phenylcarbamate, 2-(4-Imidazolyl)-1-(carbonyl-Asp-CH<sub>2</sub>F)ethyl *N*-phenylcarbamate, 2-Phenyl-1-(carbonyl-Asp-CH<sub>2</sub>F)ethyl *N*-phenylcarbamate, 2-Methyl-1-(carbonyl-Asp-CH<sub>2</sub>F)butyl *N*-phenylcarbamate, 3-Methyl-1-(carbonyl-Asp-CH<sub>2</sub>F)butyl *N*-phenylcarbamate, 1-Phenyl-1-(carbonyl-Asp-CH<sub>2</sub>F)methyl *N*-phenylcarbamate, 1-(2-Chlorophenyl)-1-(carbonyl-Asp-CH<sub>2</sub>F)methyl *N*-phenylcarbamate, 1-(4-Chlorophenyl)-1-(carbonyl-Asp-CH<sub>2</sub>F)methyl *N*-phenylcarbamate, 1-Cyclohexyl-1-(carbonyl-Asp-CH<sub>2</sub>F)methyl *N*-phenylcarbamate, 2-Chloro-1-(carbonyl-Asp-CH<sub>2</sub>F)ethyl *N*-phenylcarbamate, 2,2,2-Trifluoro-1-(carbonyl-Asp-CH<sub>2</sub>F)ethyl *N*-phenylcarbamate or *Z*-Valine 2-methyl-1-(carbonyl-Asp-CH<sub>2</sub>F)propyl ester.

Claim 25 (original). The method of claim 1, wherein said caspase inhibitor has the formula VII:



or a pharmaceutically acceptable salt thereof;

wherein R<sub>1</sub> is an optionally substituted alkyl or hydrogen;

R<sub>2</sub> is hydrogen or optionally substituted alkyl;

R<sub>3</sub> is an alkyl, saturated carbocyclic, partially saturated carbocyclic, aryl, saturated heterocyclic, partially saturated heterocyclic or heteroaryl group, wherein said group is optionally substituted;

X is O, S, NR<sub>4</sub>, or (CR<sub>4</sub>R<sub>5</sub>)<sub>n</sub>, where R<sub>4</sub> and R<sub>5</sub> are, at each occurrence, independently selected from the group consisting of hydrogen, alkyl and cycloalkyl, and n is 0, 1, 2, or 3; or

X is NR<sub>4</sub>, and R<sub>3</sub> and R<sub>4</sub> are taken together with the nitrogen atom to which they are attached to form a saturated heterocyclic, partially saturated heterocyclic or heteroaryl group, wherein said group is optionally substituted; or

X is CR<sub>4</sub>R<sub>5</sub>, and R<sub>3</sub> and R<sub>4</sub> are taken together with the carbon atom to which they are attached to form a saturated carbocyclic, partially saturated carbocyclic, aryl, saturated heterocyclic, partially saturated heterocyclic or oxygen-containing heteroaryl group, wherein said group is optionally substituted; and

Y is a residue of a natural or non-natural amino acid;

provided that when X is O, then R<sub>3</sub> is not unsubstituted benzyl or *t*-butyl; and when X is CH<sub>2</sub>, then R<sub>3</sub> is not hydrogen.

Claim 26 (withdrawn). The method of claim 25, wherein said caspase inhibitor is 2-Chlorobenzoyloxycarbonyl-Val-Asp-fmk, 3-Chlorobenzoyloxycarbonyl-Val-Asp-fmk, 4-Chlorobenzoyloxycarbonyl-Val-Asp-fmk, Phenethoxycarbonyl-Val-Asp-fmk, Cyclohexylmethoxycarbonyl-Val-Asp-fmk, Methoxycarbonyl-Val-Asp-fmk, Ethoxycarbonyl-Val-Asp-fmk, Isopropylloxycarbonyl-Val-Asp-fmk, 2-Chlorobenzoyloxycarbonyl-Ile-Asp-fmk, 3-Chlorobenzoyloxycarbonyl-Ile-Asp-fmk, 4-Chlorobenzoyloxycarbonyl-Ile-Asp-fmk, Phenylacetyl-Val-Asp-fmk, 4-Nitrobenzoyloxycarbonyl-Val-Asp-fmk, 2,5-Dimethylbenzoyloxycarbonyl-Val-Asp-fmk, 3,4-Dichlorobenzoyloxycarbonyl-Val-Asp-fmk, 3,5-Dichlorobenzoyloxycarbonyl-Val-Asp-fmk, 2,5-Dichlorobenzoyloxycarbonyl-Val-Asp-fmk, 2,6-Dichlorobenzoyloxycarbonyl-Val-Asp-fmk, 2,4-Dichlorobenzoyloxycarbonyl-Val-Asp-fmk, 2,4-Dimethylbenzoyloxycarbonyl-Val-Asp-fmk, 4-Ethylbenzoyloxycarbonyl-Val-Asp-fmk, 4-Bromobenzoyloxycarbonyl-Val-Asp-fmk, 4-Fluorobenzoyloxycarbonyl-Val-Asp-fmk, Cyclopentylmethoxycarbonyl-Val-Asp-fmk, 4-Trifluoromethylbenzoyloxycarbonyl-Val-Asp-fmk, 3-Phenylpropionyl-Val-Asp-fmk, Benzylaminocarbonyl-Val-Asp-fmk, 3-Phenylpropylloxycarbonyl-Val-Asp-fmk, 2,4-

Difluorobenzyloxycarbonyl-Val-Asp-fmk, 3,4-Difluorobenzyloxycarbonyl-Val-Asp-fmk, 4-Morpholinecarbonyl-Val-Asp-fmk, 4-Pyridylmethoxycarbonyl-Val-Asp-fmk, 2-Pyridylmethoxycarbonyl-Val-Asp-fmk, 2,6-Dichlorobenzyloxycarbonyl-Val-Asp-DCB-methylketone, Isobutoxycarbonyl-Val-Asp-fmk, Propionyl-Val-Asp-fmk, Benzyl-glutaryl-Val-Asp-fmk, Glutaryl-Val-Asp-fmk, 3-(2-Phenyloxyphenyl)propionyl-Val-Asp-fmk, 3-(5-Bromo-2-hydroxyphenyl)propionyl-Val-Asp-fmk, 3-Fluorobenzyloxycarbonyl-Val-Asp-fmk, 2-Fluorobenzyloxycarbonyl-Val-Asp-fmk, 3-Methylbenzyloxycarbonyl-Val-Asp-fmk, 2-Chloro-4-fluorobenzyloxycarbonyl-Val-Asp-fmk, 2-Naphthylmethoxycarbonyl-Val-Asp-fmk, *p*-Toluenesulfonyl-Val-Asp-fmk or *p*-Toluenesulfonyl-Phe-Asp-fmk.